PALM INTRANET

Day : Friday
Date: 10/21/2005

Time: 17:47:17

Inventor Name Search

Enter the **first few letters** of the Inventor's Last Name.
Additionally, enter the **first few letters** of the Inventor's First name.

Last Name	First Name	
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Date: 10/21/2005

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Inventor Name Search

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lefevre	f	Search

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Day : Friday
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Inventor Name Search

Enter the **first few letters** of the Inventor's Last Name.
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Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	0	"DNA shuffle" and "15 nucleotide"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 15:54
L2	0	"DNA shuffle" and (("10" or "11" or "12" or "13" or "14") near2 nucleotide$)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 15:57
L3	11516	(DNA near3 RNA) SAME hybrid	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 15:57
L4	1	l3 and "DNA shuffle"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 15:58
L5	1	("DNA/RNA" or "DNA-RNA")and "DNA shuffle"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 15:59
L6	600	"DNA/RNA" and heteroduplex	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 15:59
L7	5	l6 and (arnold.in. or stemmer.in.)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 16:03
L8	2	"6303344".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 16:03
L9	575	("T4" or "T7") near5 endonuclease	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 16:05
L10	0	l9 and "DNA shuffle"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 16:04
L11	1	l9 and (arnold.in. or stemmer.in. or crameri.in. or patten.in.)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 16:04
L12	33	l9 and (fragment with recombination)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 16:07

L13	75741	DNA near5 fragment$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 16:08
L14	113	l9 SAME l13	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 16:08
L15	0	l14 and shuffle	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 16:08
L16	45	l14 and recombination	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 16:08
S1	3334	"DNA shuffling"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:48
S2	2430	"mismatch repair" or "base excision repair"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:48
S3	290	S1 and S2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:48
S4	52	S3 and heteroduplex	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:50
S5	14757	DNase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:50
S6	46287	"restriction enzymes"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:50
S7	31219	"15 nucleotides" or "15 residues" or "15mer" or "15 bases"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:51
S8	0	denautr$ SAME hybridiz$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:52

S9	24571	denatur$ SAME hybridiz$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:52
S10	1422	"t4" WITH endonucleas$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:53
S11	36019	endonucleas$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:53
S12	68653	DAM or muts or mutl or mutH or exonuclease or helicase or SSB or "POL III" or "polymerase III"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:56
S13	290	S1 and S2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:56
S14	202	S13 and S5	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:56
S15	196	S14 and S6	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:56
S16	143	S15 and S9	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:56
S17	7	S16 and S10	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:56
S18	135	S16 and S11	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:56
S19	133	S18 and S12	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:56
S20	303	heteroduplex SAME homolog$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:57

S21	8	S19 and S20	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/21 16:57
S22	1433	dupret.in. or lefevre.in. or fourage. in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 17:30
S23	16	S22 and shuffling	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 17:40
S24	6	S23 and "Dnase"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 17:40
S25	6	S24 and fragmenting	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 17:56
S26	2	S25 and heteroduplex	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 17:40
S27	3907	"DNA shuffling"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S28	2782	"mismatch repair" or "base excision repair"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S29	368	S27 and S28	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S30	61	S29 and heteroduplex	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S31	16827	DNase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S32	51829	"restriction enzymes"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47

S33	34219	"15 nucleotides" or "15 residues" or "15mer" or "15 bases"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S34	0	denautr$ SAME hybridiz$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S35	27709	denatur$ SAME hybridiz$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S36	1541	"t4" WITH endonucleas$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S37	40218	endonucleas$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S38	74373	DAM or muts or mutl or mutH or exonuclease or helicase or SSB or "POL III" or "polymerase III"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S39	368	S27 and S28	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S40	249	S39 and S31	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S41	240	S40 and S32	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S42	177	S41 and S35	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S43	9	S42 and S36	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S44	169	S42 and S37	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47

S45	166	S44 and S38	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S46	344	heteroduplex SAME homolog$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S47	9	S45 and S46	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/19 17:47
S48	2	S23 and "repair system"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 17:59
S49	109	"WO 99/29902"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 18:03
S50	0	"WO 199929902"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 17:59
S51	61	S49 and "DNA repair"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 18:00
S52	61	S51 and shuffl$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 18:00
S53	5	"WO99/29902"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 18:15
S54	34379	arnold.in. or shao.in. or volkov.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 18:16
S55	13	S54 and heteroduplexes	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 18:43
S56	3999	DNA near2 shuffl$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 18:43

S57	8	S56 and "DNA repair system"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 19:16
S58	8	S57 and (ligase or polymerase)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 19:16
S59	1	S58 and "t4 endonuclease"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 19:17
S60	1	S58 and "T7 endonuclease"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 19:18
S61	7	S58 and mismatch	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 19:18
S62	6	S58 and "mismatch repair"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 19:19
S63	6	S58 and "DNA ligase"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 19:20
S64	1	S58 and "dITP"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 19:20
S65	0	S58 and "uracil glycosylase"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 19:20
S66	1238	uracil near2 glycosylase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 19:20
S67	1	S58 and S66	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/19 19:20
S68	5	"5556750".in. or "5605793".pn. or "5830721".pn. or "5965408".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:19

S69	5	S68 and (DNA repair)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:45
S70	2	S69 and Dnase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:21
S71	3914	"DNA shuffling"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S72	2788	"mismatch repair" or "base excision repair"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S73	369	S71 and S72	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S74	61	S73 and heteroduplex	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S75	16869	DNase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S76	51932	"restriction enzymes"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S77	34279	"15 nucleotides" or "15 residues" or "15mer" or "15 bases"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S78	0	denautr$ SAME hybridiz$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S79	27764	denatur$ SAME hybridiz$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S80	1543	"t4" WITH endonucleas$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25

S81	40305	endonucleas$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S82	74462	DAM or muts or mutl or mutH or exonuclease or helicase or SSB or "POL III" or "polymerase III"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S83	369	S71 and S72	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S84	249	S83 and S75	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S85	240	S84 and S76	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S86	177	S85 and S79	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S87	9	S86 and S80	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S88	169	S86 and S81	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S89	166	S88 and S82	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S90	345	heteroduplex SAME homolog$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S91	9	S89 and S90	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S92	1433	dupret.in. or lefevre.in. or fourage.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25

S93	16	S92 and shuffling	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S94	6	S93 and "Dnase"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S95	6	S94 and fragmenting	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S96	2	S95 and heteroduplex	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S97	6	S94 and fragmenting	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S98	3914	"DNA shuffling"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S99	2788	"mismatch repair" or "base excision repair"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S100	369	S98 and S99	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S101	16869	DNase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S102	51932	"restriction enzymes"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S103	34279	"15 nucleotides" or "15 residues" or "15mer" or "15 bases"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S104	0	denautr$ SAME hybridiz$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25

S10 5	27764	denatur$ SAME hybridiz$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S10 6	1543	"t4" WITH endonucleas$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S10 7	40305	endonucleas$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S10 8	74462	DAM or muts or mutl or mutH or exonuclease or helicase or SSB or "POL III" or "polymerase III"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S10 9	369	S98 and S99	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S11 0	249	S109 and S101	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S11 1	240	S110 and S102	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S11 2	177	S111 and S105	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S11 3	9	S112 and S106	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S11 4	169	S112 and S107	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S11 5	166	S114 and S108	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S11 6	345	heteroduplex SAME homolog$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25

S117	61	S100 and heteroduplex	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S118	9	S115 and S116	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/20 13:25
S119	2	S93 and "repair system"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S120	0	"WO 199929902"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S121	109	"WO 99/29902"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S122	61	S121 and "DNA repair"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S123	61	S122 and shuffl$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S124	5	"WO99/29902"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S125	34398	arnold.in. or shao.in. or volkov.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S126	13	S125 and heteroduplexes	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S127	4008	DNA near2 shuffl$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S128	8	S127 and "DNA repair system"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25

S129	8	S128 and (ligase or polymerase)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S130	1	S129 and "t4 endonuclease"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S131	1	S129 and "T7 endonuclease"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S132	7	S129 and mismatch	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S133	6	S129 and "mismatch repair"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S134	6	S129 and "DNA ligase"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S135	1	S129 and "dITP"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S136	0	S129 and "uracil glycosylase"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S137	1240	uracil near2 glycosylase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S138	1	S129 and S137	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:25
S139	0	S69 and "serum albumin"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:45
S140	0	S69 and "albumin"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:46

S14 1	0	S69 and "sperm"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:46
S14 2	2815	S71 and "albumin"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:46
S14 3	1	S142 and "fragmentation assay"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:56
S14 4	10	dupret.in. and "DNA shuffling"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:57
S14 5	16	dupret.in. and "shuffling"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 13:59
S14 6	3	S145 and "DNA repair"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 14:00
S14 7	3	S145 and (DAM or methylase or muts or mutl or mutH or exonulcease or helicase or SB)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 16:15
S14 8	2	"6376246".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 16:16
S14 9	4	"646224".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 16:16
S15 0	2	"6426224".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 16:39
S15 1	8	carr.in. and patten.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 16:40
S15 2	5	S151 and "repair"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 16:54

S153	2	"6537746".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 18:32
S154	12	"exposed" near7 "repair system"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/20 18:33
S155	3	S154 and heteroduplex	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/10/21 15:53

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 FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 17:33:19 ON 21 OCT 2005
L1              0 S "DNA SHUFFLING" OF "DIRECTED EVOLUTION"
L2              0 S "DNA SHUFFLING" RF "DIRECTED EVOLUTION"
L3           2066 S "DNA SHUFFLING" OR  "DIRECTED EVOLUTION"
L4          38576 S STEMMER?/AU OR ARNOLD?/AU OR DUPRET?/AU OR LEFEVRE?/AU OR FOU
L5          35257 S DNASE
L6           2285 S URACIL (5W) GLYCOSYLASE
L7          55014 S ENDONUCLEASE
L8           2188 S DNA REPAIR ENZYME
L9          76567 S DNA REPAIR
L10           233 S L3 AND L4
L11             1 S L10 AND L9
L12             0 S L3 AND L8
L13            11 S L3 AND L9
L14             8 DUP REM L13 (3 DUPLICATES REMOVED)
L15          3135 S "REPAIR SYSTEM" AND DNA
L16           270 S DAM (2W) METHYLASE
L17        292387 S RNA-DNA OR "RNA/DNA" OR "DNA/RNA" OR DNA-RNA OR (DNA (3W) RNA
L18            29 S L17 AND L3
L19            10 S L18 NOT PY>=2002
L20            17 S L18 NOT PY>=2003
L21            12 DUP REM L20 (5 DUPLICATES REMOVED)
L22           334 S L4 AND L17
L23        131036 S L22 AND L3 OR RECOMBINATION
L24        132740 S L3 OR RECOMBINATION
L25             6 S L22 AND L24
L26             6 DUP REM L25 (0 DUPLICATES REMOVED)
L27         34534 S DNA (3W) FRAGMENTATION
L28            23 S L27 AND SHUFFLING
L29             4 S L28 AND L5
L30             2 DUP REM L29 (2 DUPLICATES REMOVED)
L31            12 S L6 AND L27
L32             7 DUP REM L31 (5 DUPLICATES REMOVED)
L33             5 S L32 NOT PY>=2003
L34         31269 S MUTS OR MUTL OR MUTH OR SSB OR DAM OR DNA LIGASE
L35             0 S (T4 OR T7) (3W) ENDOCULEASE
L36          1238 S (T4 OR T7) (3W) ENDONUCLEASE
L37             0 S L36 AND L27
L38             0 S L36 AND L4
L39             0 S L36 AND L27
L40             0 S L16 AND L27
L41           362 S L15 AND L34
L42            73 S L41 AND L23
L43            60 S L42 NOT PY>=2003
L44            28 DUP REM L43 (32 DUPLICATES REMOVED)
L45             0 S L44 AND L4
L46      10064105 S 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 20 OR 30
L47         28507 S L46 (2W) (RESIDUE OR NUCLEOTIDE OR BP)
L48            34 S L47 AND L27
L49            29 S L48 NOT PY>=2003
L50            15 DUP REM L49 (14 DUPLICATES REMOVED)

=>
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L11 ANSWER 1 OF 1 MEDLINE on STN
ACCESSION NUMBER: 1999403372 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10471748
TITLE: Recombination and chimeragenesis by in vitro heteroduplex formation and in vivo repair.
AUTHOR: Volkov A A; Shao Z; **Arnold F H**
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering 210-41, California Institute of Technology, Pasadena, CA 91125, USA.
SOURCE: Nucleic acids research, (1999 Sep 15) 27 (18) e18.
Journal code: 0411011. ISSN: 1362-4962.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 20010521
Entered Medline: 19990915

AB We describe a simple method for creating libraries of chimeric DNA sequences derived from homologous parental sequences. A heteroduplex formed in vitro is used to transform bacterial cells where repair of regions of non-identity in the heteroduplex creates a library of new, recombined sequences composed of elements from each parent. Heteroduplex recombination provides a convenient addition to existing DNA recombination methods ('**DNA shuffling**') and should be particularly useful for recombining large genes or entire operons. This method can be used to create libraries of chimeric polynucleotides and proteins for **directed evolution** to improve their properties or to study structure-function relationships. We also describe a simple test system for evaluating the performance of DNA recombination methods in which recombination of genes encoding truncated green fluorescent protein (GFP) reconstructs the full-length gene and restores its characteristic fluorescence. Comprising seven truncated GFP constructs, this system can be used to evaluate the efficiency of recombination between mismatches separated by as few as 24 bp and as many as 463 bp. The optimized heteroduplex recombination protocol is quite efficient, generating nearly 30% fluorescent colonies for recombination between two genes containing stop codons 463 bp apart (compared to a theoretical limit of 50%).

=>

L14 ANSWER 1 OF 8 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005283542 EMBASE

TITLE: Fast **directed evolution** of non-immunoglobulin proteins by somatic hypermutation in immune cells.

AUTHOR: Heinis C.; Johnsson K.

CORPORATE SOURCE: Dr. C. Heinis, Institute of Chemical Sciences and Engineering, Ecole Polytechnique Federale de Lausanne (EPFL), 1015 Lausanne, Switzerland. christian.heinis@epfl.ch

SOURCE: ChemBioChem, (2005) Vol. 6, No. 5, pp. 804-806.
Refs: 15
ISSN: 1439-4227 CODEN: CBCHFX

COUNTRY: Germany

DOCUMENT TYPE: Journal; (Short Survey)

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20050714
Last Updated on STN: 20050714

AB New, improved phenotypes. Somatic hypermutation in immune cells can be used for the fast **directed evolution** of proteins other than immunoglobulins (e.g., autofluorescent proteins). The target gene is inserted into the genome of activated B lymphocytes where it is mutated. Cells expressing a desired phenotype are selected and subjected to further evolution cycles to accumulate beneficial mutations. .COPYRGT. 2005 Wiley-VCH Verlag GmbH & Co. KGaA.

L14 ANSWER 2 OF 8 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005386488 EMBASE

TITLE: Evolving phage vectors for cell targeted gene delivery - An update.

AUTHOR: Larocca D.; Burg M.A.; Baird A.

CORPORATE SOURCE: D. Larocca, Selective Genetics, Inc., 11588 Sorrento Valley Road, San Diego, CA 92121, United States. laroccad@cox.net

SOURCE: Medicinal Chemistry Reviews - Online, (2005) Vol. 2, No. 2, pp. 111-114.
Refs: 23
ISSN: 1567-2700
URL: http://saturn.bids.ac.uk/cgi-bin/ds_deliver/1/u/d/ISIS/20782636.1/ben/mcro/2005/00000002/00000002/art00002/91C5FA2CD50BFC791124696316B30773A8CDD24CB9.pdf?link=http://www.ingentaconnect.com/error/delivery&format=pdf

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 022 Human Genetics
030 Pharmacology
037 Drug Literature Index
039 Pharmacy

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20051006
Last Updated on STN: 20051006

AB Bacteriophage vectors are an attractive alternative to synthetic and animal viral gene delivery vectors. We have demonstrated that ligand targeted bacteriophage particles can be used to deliver a functional transgene to mammalian cells that bear the appropriate receptors. Because transduction of mammalian cells by untargeted phage is negligible, the specificity of phage-mediated gene delivery can be determined by the choice of targeting ligand that is displayed on the phage surface. Thus, phage display vectors can potentially be targeted genetically for gene delivery to specific cells in the body with little or no delivery to non-targeted cells. Moreover, since bacteriophage have not evolved to replicate in mammalian cells they are not likely to have toxicity problems

associated with many animal viral vectors. Although the efficiency of phage-mediated gene delivery has been low compared to animal viral vectors, studies demonstrating increased gene transfer using agents that stimulate **DNA repair** indicate the potential for improving phage-mediated gene delivery. Indeed, the same principles of phage display that have been applied extensively to the **directed evolution** of binding ligands can now be applied to the adaptation of the phage particles, themselves for safe and effective therapeutic gene delivery. .COPYRGT. 2005 Bentham Science Publishers Ltd.

L14 ANSWER 3 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2003206076 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12725859
TITLE: **Directed evolution** of O6-alkylguanine-DNA alkyltransferase for efficient labeling of fusion proteins with small molecules in vivo.
AUTHOR: Juillerat Alexandre; Gronemeyer Thomas; Keppler Antje; Gendreizig Susanne; Pick Horst; Vogel Horst; Johnsson Kai
CORPORATE SOURCE: Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology, CH-1015 Lausanne, Switzerland.
SOURCE: Chemistry & biology, (2003 Apr) 10 (4) 313-7.
Journal code: 9500160. ISSN: 1074-5521.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20030503
Last Updated on STN: 20031217
Entered Medline: 20050105

AB We report here the generation of mutants of the human O(6)-alkylguanine-DNA alkyltransferase (hAGT) for the efficient in vivo labeling of fusion proteins with synthetic reporter molecules. Libraries of hAGT were displayed on phage, and mutants capable of efficiently reacting with the inhibitor O(6)-benzylguanine were selected based on their ability to irreversibly transfer the benzyl group to a reactive cysteine residue. Using synthetic O(6)-benzylguanine derivatives, the selected mutant proteins allow for a highly efficient covalent labeling of hAGT fusion proteins in vivo and in vitro with small molecules and therefore should become important tools for studying protein function in living cells. In addition to various applications in proteomics, the selected mutants also yield insight into the interaction of the **DNA repair** protein hAGT with its inhibitor O(6)-benzylguanine.

L14 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:534398 BIOSIS
DOCUMENT NUMBER: PREV200300536459
TITLE: Protein chemistry in living cells.
AUTHOR(S): Johnsson, Kai [Reprint Author]
CORPORATE SOURCE: Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology Lausanne, BCH, Lausanne, CH-1015, Switzerland
kai.johnsson@epfl.ch
SOURCE: Abstracts of Papers American Chemical Society, (2003) Vol. 226, No. 1-2, pp. ORGN 695. print.
Meeting Info.: 226th ACS (American Chemical Society) National Meeting. New York, NY, USA. September 07-11, 2003. American Chemical Society.
ISSN: 0065-7727 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Nov 2003
Last Updated on STN: 12 Nov 2003

L14 ANSWER 5 OF 8 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001424931 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11472942
TITLE: Rapid evolution of novel traits in microorganisms.
AUTHOR: Selifonova O; Valle F; Schellenberger V
CORPORATE SOURCE: Genencor International, Inc., Palo Alto, California 94304, USA.
SOURCE: Applied and environmental microbiology, (2001 Aug) 67 (8) 3645-9.
Journal code: 7605801. ISSN: 0099-2240.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011029
Last Updated on STN: 20011029
Entered Medline: 20011025

AB The use of natural microorganisms in biotransformations is frequently constrained by their limited tolerance to the high concentrations of metabolites and solvents required for effective industrial production. In many cases, more robust strains have to be generated by random mutagenesis and selection. This process of **directed evolution** can be accelerated in mutator strains, which carry defects in one or more of their **DNA repair** genes. However, in order to use mutator strains, it is essential to restore the normal low mutation rate of the selected organisms immediately after selection to prevent the accumulation of undesirable spontaneous mutations. To enable this process, we constructed temperature-sensitive plasmids that temporarily increase the mutation frequency of their hosts by 20- to 4,000-fold. Under appropriate selection pressure, microorganisms transformed with mutator plasmids can be quickly evolved to exhibit new, complex traits. By using this approach, we were able to increase the tolerance of three bacterial strains to dimethylformamide by 10 to 20 g/liter during only two subsequent transfers. Subsequently, the evolved strains were returned to their normal low mutation rate by curing the cells of the mutator plasmids. Our results demonstrate a new and efficient method for rapid strain improvement based on in vivo mutagenesis.

L14 ANSWER 6 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2001517249 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11564555
TITLE: **Directed evolution** to increase camptothecin sensitivity of human DNA topoisomerase I.
AUTHOR: Scaldaferro S; Tinelli S; Borgnetto M E; Azzini A; Capranico G
CORPORATE SOURCE: Department of Experimental Oncology, Istituto Nazionale Tumori, Milan, Italy.
SOURCE: Chemistry & biology, (2001 Sep) 8 (9) 871-81.
Journal code: 9500160. ISSN: 1074-5521.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20010924
Last Updated on STN: 20020125
Entered Medline: 20020110

AB BACKGROUND: Human DNA topoisomerase I (top1) relaxes DNA supercoiling during basic nuclear processes. The enzyme is the main target of antitumor agents, such as camptothecins (CPT), that transform top1 into a DNA-damaging agent. RESULTS: By **directed evolution** of a C-terminal portion, we selected human top1 mutants that were 22-28-fold more CPT-sensitive than wild-type top1 in Saccharomyces cerevisiae cells. The evolved enzymes showed unique mutation patterns and were more processive in plasmid relaxation assays. A top1 mutant had only two amino acid changes in the linker domain, one of which may change a linker/core domain contact surface. The mutant stimulated DNA cleavage to higher levels than the wild-type enzyme and was more sensitive to CPT in a cleavage assay. Moreover, the mutant was more CPT-sensitive than

wild-type top1 in a repair-deficient yeast strain. CONCLUSIONS: Mutations in the linker domain can affect DNA binding and CPT sensitivity of human top1. Such drug-hypersensitive topoisomerases may be useful in developing DNA cutters with high cell lethality and in new drug discovery programs.

L14 ANSWER 7 OF 8 MEDLINE on STN
ACCESSION NUMBER: 1999403372 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10471748
TITLE: Recombination and chimeragenesis by in vitro heteroduplex formation and in vivo repair.
AUTHOR: Volkov A A; Shao Z; Arnold F H
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering 210-41, California Institute of Technology, Pasadena, CA 91125, USA.
SOURCE: Nucleic acids research, (1999 Sep 15) 27 (18) e18.
Journal code: 0411011. ISSN: 1362-4962.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 20010521
Entered Medline: 19990915

AB We describe a simple method for creating libraries of chimeric DNA sequences derived from homologous parental sequences. A heteroduplex formed in vitro is used to transform bacterial cells where repair of regions of non-identity in the heteroduplex creates a library of new, recombined sequences composed of elements from each parent. Heteroduplex recombination provides a convenient addition to existing DNA recombination methods ('**DNA shuffling**') and should be particularly useful for recombining large genes or entire operons. This method can be used to create libraries of chimeric polynucleotides and proteins for **directed evolution** to improve their properties or to study structure-function relationships. We also describe a simple test system for evaluating the performance of DNA recombination methods in which recombination of genes encoding truncated green fluorescent protein (GFP) reconstructs the full-length gene and restores its characteristic fluorescence. Comprising seven truncated GFP constructs, this system can be used to evaluate the efficiency of recombination between mismatches separated by as few as 24 bp and as many as 463 bp. The optimized heteroduplex recombination protocol is quite efficient, generating nearly 30% fluorescent colonies for recombination between two genes containing stop codons 463 bp apart (compared to a theoretical limit of 50%).

L14 ANSWER 8 OF 8 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 96063643 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7488146
TITLE: The **directed evolution** of radiation resistance in E. coli.
AUTHOR: Ewing D
CORPORATE SOURCE: Department of Radiation Oncology and Nuclear Medicine, Medical College of Pennsylvania, Philadelphia 19102, USA.
SOURCE: Biochemical and biophysical research communications, (1995 Nov 13) 216 (2) 549-53.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE).
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19970203
Entered Medline: 19951221

AB E. coli AB1157 (a wild-type, K-12 strain having no known defects in **DNA repair** capability) was irradiated daily with a very large X-ray dose to develop a series of strains unusually resistant to both X rays and ultraviolet (UV) photons. An understanding of how

wild-type strains mutate and become more resistant should lead to a better understanding of **DNA repair** processes and their effects on radiation sensitivity.

=>

L30 ANSWER 1 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2002728680 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12490730
TITLE: Random **DNA fragmentation** with endonuclease V: application to DNA **shuffling**.
AUTHOR: Miyazaki Kentaro
CORPORATE SOURCE: Institute for Biological Resources and Functions, National Institute of Advanced Industrial Science and Technology (AIST), Central 6, 1-1-1 Higashi, Tsukuba, Ibaraki 305-8566, Japan.. miyazaki-kentaro@aist.go.jp
SOURCE: Nucleic acids research, (2002 Dec 15) 30 (24) e139.
Journal code: 0411011. ISSN: 1362-4962.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20021220
Last Updated on STN: 20030308
Entered Medline: 20030307
AB The enzyme endonuclease V nicks uracil-containing DNA at the second or third phosphodiester bond 3' to uracil sites. I applied the enzyme to random fragmentation of DNA to revise the complex DNA **shuffling** protocol. The merit of using endonuclease V is that cleavage occurs at random sites and the length of the fragments can easily be adjusted by varying the concentration of dUTP in the polymerase chain reaction. Unlike the conventional method using **DNase** I, no partial digestion or gel separation of fragments is required. Therefore, labor is dramatically reduced and reproducibility ensured. I applied this method to recombine two truncated green fluorescent protein (GFP) genes and demonstrated successful DNA **shuffling** by the appearance of the fluorescent full-length GFP genes.

L30 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 95024192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7938023
TITLE: **DNA shuffling** by random **fragmentation** and reassembly: in vitro recombination for molecular evolution.
AUTHOR: Stemmer W P
CORPORATE SOURCE: Affymax Research Institute, Palo Alto, CA 94304.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994 Oct 25) 91 (22) 10747-51.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941123
AB Computer simulations of the evolution of linear sequences have demonstrated the importance of recombination of blocks of sequence rather than point mutagenesis alone. Repeated cycles of point mutagenesis, recombination, and selection should allow in vitro molecular evolution of complex sequences, such as proteins. A method for the reassembly of genes from their random DNA fragments, resulting in in vitro recombination is reported. A 1-kb gene, after **DNase** I digestion and purification of 10- to 50-bp random fragments, was reassembled to its original size and function. Similarly, a 2.7-kb plasmid could be efficiently reassembled. Complete recombination was obtained between two markers separated by 75 bp; each marker was located on a separate gene. Oligonucleotides with 3' and 5' ends that are homologous to the gene can be added to the fragment mixture and incorporated into the reassembled gene. Thus, mixtures of synthetic oligonucleotides and PCR fragments can be mixed into a gene at defined positions based on homology. As an example, a library of chimeras

of the human and murine genes for interleukin 1 beta has been prepared. **Shuffling** can also be used for the in vitro equivalent of some standard genetic manipulations, such as a backcross with parental DNA. The advantages of recombination over existing mutagenesis methods are likely to increase with the numbers of cycles of molecular evolution.

=>

L50 ANSWER 12 OF 15 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 95024192 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7938023

TITLE: **DNA** shuffling by random **fragmentation** and reassembly: in vitro recombination for molecular evolution.

AUTHOR: Stemmer W P

CORPORATE SOURCE: Affymax Research Institute, Palo Alto, CA 94304.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1994 Oct 25) 91 (22) 10747-51.
Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199411

ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941123

AB Computer simulations of the evolution of linear sequences have demonstrated the importance of recombination of blocks of sequence rather than point mutagenesis alone. Repeated cycles of point mutagenesis, recombination, and selection should allow in vitro molecular evolution of complex sequences, such as proteins. A method for the reassembly of genes from their random DNA fragments, resulting in in vitro recombination is reported. A 1-kb gene, after DNase I digestion and purification of **10-** to 50-**bp** random fragments, was reassembled to its original size and function. Similarly, a 2.7-kb plasmid could be efficiently reassembled. Complete recombination was obtained between two markers separated by 75 bp; each marker was located on a separate gene. Oligonucleotides with 3' and 5' ends that are homologous to the gene can be added to the fragment mixture and incorporated into the reassembled gene. Thus, mixtures of synthetic oligonucleotides and PCR fragments can be mixed into a gene at defined positions based on homology. As an example, a library of chimeras of the human and murine genes for interleukin 1 beta has been prepared. Shuffling can also be used for the in vitro equivalent of some standard genetic manipulations, such as a backcross with parental DNA. The advantages of recombination over existing mutagenesis methods are likely to increase with the numbers of cycles of molecular evolution.